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August 14, 1995

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ATTN: TSCA Section 8(e) Submission

- Ref: 1. [] facsimiles to [], dated August 8 and 11, Re: Four Week Oral Toxicity Study In The Rat With Two Week Recovery Period With [] (Follow-up histopathology results), received August 8, 1995.
2. My letter to you dated August 6, 1995, Re: TSCA Section 8(e) Submission.

Dear Sirs:

As a follow-up to our draft tables of the TSCA Section 8(e) Submission (Ref. 2), we are submitting the enclosed histopathological results (Ref. 1.) for your review.

The follow-up tables indicate more complete histopathology results of the four week rat oral toxicity study performed on the following R&D material currently being researched by []:

Specific chemical name: Benzenebutanenitrile, α,α,γ -trimethyl
Chemical Abstract Service number: 75490-39-0

The initial histopathological findings which were reported in my letter of August 6, 1995 (Ref. 2) indicated seminiferous tubular atrophy at the highest dose level in the four week study. However, as noted in the attached follow-up results, the negative control groups achieved a similar level of seminiferous tubular atrophy indicating that the findings in the treatment groups are not test-article related.

Based on the initial interim report results, we had modified our MSDS to reflect the seminiferous tubular atrophy. As a result of the follow-up histopathological data, this effect is not considered significant and will not be noted on the MSDS. Following good general industrial hygiene practices, we will continue to advise the use of splash goggles or face shield when eye contact might occur, use of chemical resistant gloves, and use of a NIOSH approved respirator when inhalation of high concentrations may occur. The ventilation would meet ACGIH criteria.

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We have included sanitized and unsanitized versions of the follow-up histopathology results and request that you maintain our company identity, references to company personnel, and company synonyms and product codes of the chemical substance in this communication as "CONFIDENTIAL BUSINESS INFORMATION".

If you have any questions or comments, please contact me at [].

[]

[]

Enclosures

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National (01480) 890431 extn 1022.

ATTENTION OF: [] FROM: []
COMPANY: [] DATE: 8 August 1995
FAX NUMBER: [] []
MESSAGE: []

Re: Four week oral toxicity study in the rat with two week recovery period with []

Examination of the histopathology extension has now been completed with a review of all original slides. A draft table of histopathological results is attached

Treatment-related changes included

Liver - a dose related incidence of centrilobular hepatocyte enlargement in male and female rats receiving 150 and 500 mg/kg/day at the end of treatment.

Centrilobular hepatocyte enlargement was also observed in a small number of male and female rats allowed a 2 week recovery period after receiving 500 mg/kg/day.

Kidney - a dose related incidence of cortical tubules with eosinophilic inclusions in male rats receiving 150 and 500 mg/kg/day at the end of treatment.

A trace degree of this change was still present in 1/5 male rats allowed a 2 week recovery period after receiving 500 mg/kg/day.

The lower incidence of liver and kidney changes among recovery rats was considered to show partial reversibility of these changes.

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Testes

Initial examination of the testes suggested a possible treatment-related increase of atrophic seminiferous tubules among males receiving 500 mg/kg/day. However examination of the testes and epididymides from all male rats on this study shows comparable incidences between treated and control groups. The greater degree of seminiferous tubular atrophy in males receiving 500 mg/kg/day compared to male controls at the end of treatment was considered to be fortuitous and not related to the test compound as the incidence and degree of this change was comparable between treated and control rats at the end of the recovery period.

The grading system used for seminiferous tubular atrophy is as follows:

Trace less than 10 tubular cross sections

Minimal up to 30 of tubular cross sections

Moderate over 30 up to 60 of tubular cross sections

Marked over 60% of tubular cross sections

If I can be of any further assistance please do not hesitate to contact me.

With kind regards

[]

[]

PATHOLOGY - INTERGROUP COMPARISON OF MICROSCOPIC FINDINGS INCIDENCE

STUDY NO: [] TITLE: TOXICITY TO RATS WITH []

	MALES					FEMALES				
	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5
ANIMALS ON STUDY	10	5	5	10	10	10	5	5	10	10
ANIMALS COMPLETED	10	5	5	10	10	10	5	5	10	10
LUNGS EXAMINED	1	0	0	0	0	0	0	0	1	1
Vascular congestion (TOTAL)	1	0	0	0	0	0	0	0	1	1
Minimal	1	0	0	0	0	0	0	0	1	1
HEART EXAMINED	6	0	0	5	5	5	0	0	6	6
NO ABNORMALITIES DETECTED	6	0	0	5	5	5	0	0	6	6
LYMPH NODES - CERVICAL EXAMINED	1	0	0	0	0	3	0	0	3	3
Necrotic pleurisy (TOTAL)	1	0	0	0	0	3	0	0	3	3
Minimal	0	0	0	0	0	3	0	0	3	3
Moderate	1	0	0	0	0	0	0	0	0	0
SPLEEN EXAMINED	2	0	0	5	5	5	0	0	6	6
NO ABNORMALITIES DETECTED	2	0	0	5	5	5	0	0	6	6
LIVER EXAMINED	10	5	5	10	10	10	5	5	10	10
NO ABNORMALITIES DETECTED	10	5	5	10	10	10	5	5	10	10
Centrilobular hepatocyte necrosis (TOTAL)	0	0	2	6	6	0	0	2	7	7
Minimal	0	0	2	6	6	0	0	2	5	5
Moderate	0	0	0	0	0	0	0	0	2	2
Extramedullary haemopoiesis (TOTAL)	0	0	0	0	0	0	0	0	1	1
Minimal	0	0	0	0	0	0	0	0	1	1
Centrilobular hepatocyte necrosis (TOTAL)	0	0	0	0	0	0	0	0	1	1
Moderate	0	0	0	0	0	0	0	0	1	1
KIDNEYS EXAMINED	10	5	5	10	10	5	0	0	6	6
NO ABNORMALITIES DETECTED	7	5	2	4	4	5	0	0	6	6



PATHOLOGY - INTERGROUP COMPARISON OF MICROSCOPIC FINDINGS INCIDENCE

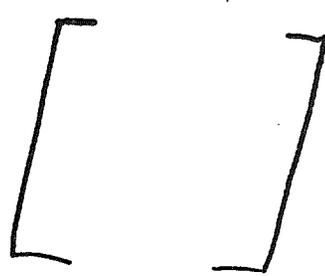
TITLE: TOXICITY TO RATS WITH []

	MALES					FEMALES				
	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5

ANIMALS ON STUDY
 ANIMALS COMPLETED

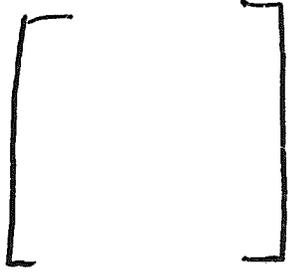
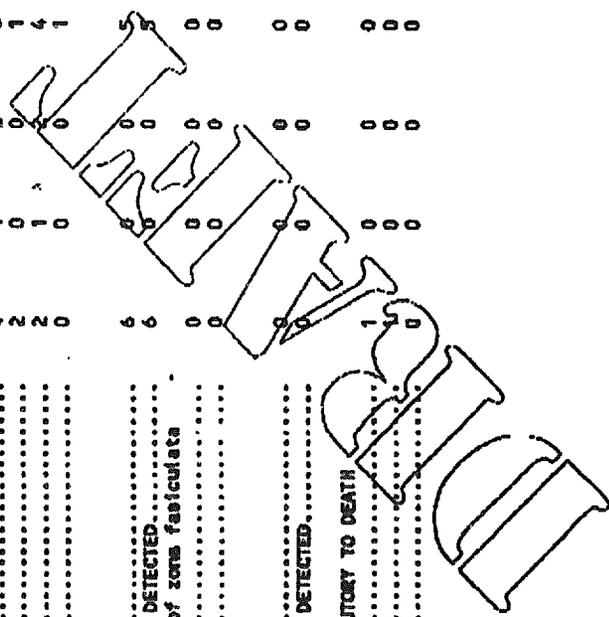
(CONTINUED)

KIDNEYS	10	5	5	10	10	10	5	5	10	10
Cortical scarring (TOTAL)	1	0	0	0	0	0	0	0	0	0
Minimal	1	0	0	0	0	0	0	0	0	0
Cortical tubules - basophilic (TOTAL)	2	0	0	0	0	0	0	0	0	0
Minimal	2	0	0	0	0	0	0	0	0	0
Cortical tubules with eosinophilic inclusions (TOTAL)	0	0	3	6	0	0	0	0	0	0
Trace	0	0	2	1	0	0	0	0	0	0
Minimal	0	0	1	0	0	0	0	0	0	0
Moderate	0	0	0	0	0	0	0	0	0	0
UTERUS	0	0	0	0	0	0	0	0	1	1
EXAMINED	0	0	0	0	0	0	0	0	1	1
Luminal distention (TOTAL)	0	0	0	0	0	0	0	0	1	1
Minimal	0	0	0	0	0	0	0	0	1	1
EPIDIDYMIDES	10	5	5	10	0	0	0	0	0	0
EXAMINED	9	5	5	9	0	0	0	0	0	0
NO ABNORMALITIES DETECTED	0	0	0	0	0	0	0	0	0	0
Reduced numbers of spermatozoa in caput (TOTAL)	1	0	0	1	0	0	0	0	0	0
Minimal	1	0	0	1	0	0	0	0	0	0
Moderate	0	0	0	0	0	0	0	0	0	0
Abnormal spermatozoa in ducts (TOTAL)	1	0	0	1	0	0	0	0	0	0
Minimal	1	0	0	1	0	0	0	0	0	0
TESTES	10	5	5	10	0	0	0	0	0	0
EXAMINED	4	4	2	4	0	0	0	0	0	0
NO ABNORMALITIES DETECTED	6	1	3	6	0	0	0	0	0	0
Seminiferous tubular atrophy (TOTAL)	3	0	0	0	0	0	0	0	0	0
Trace	2	0	0	0	0	0	0	0	0	0
Minimal	0	0	0	0	0	0	0	0	0	0
Moderate	1	0	0	0	0	0	0	0	0	0
Marked	0	0	0	0	0	0	0	0	0	0



P A T H O L O G Y - INTERGROUP COMPARISON OF MICROSCOPIC FINDINGS INCIDENCE
 STUDY NO: [] TITLE: TOXICITY TO RATS WITH []

	GROUP	GROUP	GROUP	GROUP	GROUP						
	1	2	3	4	5	6	7	8	9	10	11
	MALES						FEMALES				
ANIMALS ON STUDY	10	5	5	10	10	10	5	5	5	10	10
ANIMALS COMPLETED	10	5	5	10	10	10	5	5	5	10	10
TESTES (CONTINUED)											
Vacuoles in seminiferous epithelium	4	1	2	6	0	0	0	0	0	0	0
(TOTAL).....	2	0	0	1	0	0	0	0	0	0	0
Trace.....	2	1	0	4	0	0	0	0	0	0	0
Minimal.....	0	0	0	1	0	0	0	0	0	0	0
Moderate.....	0	0	0	0	0	0	0	0	0	0	0
ADRENALS											
EXAMINED.....	6	0	0	5	5	5	0	0	0	6	5
NO ABNORMALITIES DETECTED.....	6	0	0	5	5	5	0	0	0	6	5
Increased width of zona fasciculata	0	0	0	0	0	0	0	0	0	1	1
(TOTAL).....	0	0	0	0	0	0	0	0	0	1	1
Minimal.....	0	0	0	0	0	0	0	0	0	1	1
CECOPHAGUS											
EXAMINED.....	0	0	0	0	0	0	0	0	0	1	1
NO ABNORMALITIES DETECTED.....	0	0	0	0	0	0	0	0	0	1	1
*FACTORS CONTRIBUTORY TO DEATH											
EXAMINED.....	1	0	0	0	0	0	0	0	0	1	1
Unknown.....	0	0	0	0	0	0	0	0	0	0	0
Accident.....	0	0	0	0	0	0	0	0	0	0	1





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ATTENTION OF: [] FROM: []
COMPANY: [] DATE: 11 August 1995
FAX NUMBER: []
MESSAGE:

Re Four week oral toxicity study in the rat with two week recovery period with []

Please find attached the microscopic pathology table for the above study that has data recorded for terminal kill and recovery kill presented separately. I can confirm that the terminal and recovery data will be presented on separate tables for all reports and that the combination of the data into one table (my fax of 8 August) was a mistake.

If I can be of any further assistance please do not hesitate to contact me.

With kind regards [] []

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2/11 # []

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TABLE I
Microscopic pathology incidence summary

Removal reason: Intercurrent	Males				Females			
	Group 1	Group 2	Group 3	Group 4	Group 1	Group 2	Group 3	Group 4
Animals on study Animals completed	10	8	5	10	10	5	5	10
Lungs Examined Vascular congestion (Total) Minimal	1	0	0	0	0	0	0	1
Heart Examined No abnormalities detected	1	0	0	0	0	0	0	1
Spleen Examined No abnormalities detected	1	0	0	0	0	0	0	1
Liver Examined No abnormalities detected Centrilobular hepatocyte necrosis (Total) Moderate	1	0	2	0	0	0	0	1
Kidneys Examined No abnormalities detected	1	0	0	0	0	0	0	1
Endocrine Examined No abnormalities detected	1	0	0	0	0	0	0	0
Testes Examined No abnormalities detected	1	0	0	0	0	0	0	0
Adrenals Examined No abnormalities detected	1	0	0	0	0	0	0	0

[] 10/8/95

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TABLE 1
(Microscopic pathology incidence summary - continued)

Removal reason: Incurrent	Males				Females			
	Group 1	Group 2	Group 3	Group 4	Group 1	Group 2	Group 3	Group 4
Animals on study Animals completed	10 1	5 0	5 0	10 0	10 0	5 0	5 0	10 1
Adrenals Increased width of zona fasciculata (Total) Minimal	0 0	1 1						
Oesophagus Examined No abnormalities detected	0 0	1 1						
Factors Contributory To Death Examined Unknown Accident	1 0	0 0	0 0	0 0	0 0	0 0	0 0	1 1

(Continued)

[] - 10/8/95

TABLE 1
(Microscopic pathology incidence summary - continued)

Removal reason: Recovery	Males				Females			
	Group 1	Group 2	Group 3	Group 4	Group 1	Group 2	Group 3	Group 4
Animals on study Animals completed	10 4	5 0	5 0	10 5	10 5	5 0	5 0	10 4
Liver Examined No abnormalities detected Centrilobular hepatocyte enlargement (Total) Minimal	4 4 0 0	0 0 0 0	0 0 0 0	5 4 1 1	5 3 0 0	0 0 0 0	0 0 0 0	4 2 2 0
Kidneys Examined No abnormalities detected Cortical scarring (Total) Minimal	4 3 1 1	0 0 0 0	0 0 0 0	5 4 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0
Cortical tubules with eosinophilic inclusions (Total) Trace	0 0	0 0	0 0	1 1	0 0	0 0	0 0	0 0
Epididymides Examined No abnormalities detected Reduced numbers of spermatozoa in caput (Total) Minimal Moderate	4 3 1 1 0	0 0 0 0 0	0 0 0 0 0	5 4 1 1 1	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0
Abnormal spermatogenic cells in ducts (Total) Minimal	1 1	0 0	0 0	1 1	0 0	0 0	0 0	0 0
Testes Examined No abnormalities detected Seminiferous tubular atrophy (Total) Trace Minimal Marked	4 1 3 1 1 1	0 0 0 0 0 0	0 0 0 0 0 0	5 2 3 0 2 1	0 0 0 0 0 0	0 0 0 0 0 0	0 0 0 0 0 0	

[] - 10/8/95

TABLE I
(Microscopic pathology incidence summary - continued)

Removal reason: Recovery	Males				Females			
	Group 1	Group 2	Group 3	Group 4	Group 1	Group 2	Group 3	Group 4
Animals on study	10	5	5	10	10	5	5	10
Animals completed	4	0	0	5	5	0	0	4
Testes Vacuoles in seminiferous epithelium (Total)	(Continued)							
Trace	3	0	0	3	0	0	0	0
Minimal	1	0	0	1	0	0	0	0
Moderate	0	0	0	1	0	0	0	0